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EXAMINER

LIN, JERRY

ART UNIT

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1631

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PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/660,434	<b>Applicant(s)</b> GLINSKII, GUENNADI V.	
	<b>Examiner</b> JERRY LIN	<b>Art Unit</b> 1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 06 November 2008.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-28 and 36-38 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-28 and 36-38 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                     | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

### **DETAILED ACTION**

1. Applicants' arguments, filed November 6, 2008, have been fully considered and they are not deemed to be persuasive. However, in light of recent court decisions, an additional rejection is also required. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

### ***Status of the Claims***

Claims 1-28 and 36-38 are under examination.

Regarding claims 24-28, the Table 69 was elected as species, and the other tables are withdrawn as being drawn to a non-elected species.

### ***Claim Rejections - 35 USC § 101***

2. 35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

3. Claims 1-28 and 36-38 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

The instant claims are drawn to a method of listing a subset of genes. However, as the method does not recite a physical transformation of matter, the method must be tied to a machine to be patentable subject matter (For further explanation see, *In Re Bilski* (No. 2007-10030, decided 10/30/2008)). In the instant case, the claimed method steps are not tied to a machine, and thus are non-statutory.

***Claim Rejections - 35 USC § 103***

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

5. Claims 1-6, 8-11, and 16-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Alizadeh et al. (Nature (2000) Volume 403, pages 503-511) in view of Bertucci et al. (Human Molecular Genetics (2000) Volume 9, Number 20, pages 2981-2991).

The instant claims are drawn to identifying a subset of genes using a correlation coefficient calculated from gene expression data.

Regarding claim 1, Alizadeh et al. teach using two samples that different with respect to phenotype and determining a reference set of genes (page 504, section under "Analysis of gene expression in lymphoid malignancies"), identifying a second reference set of expressed genes independent of the first reference set from a third and fourth sample where the third or fourth sample is from a different source than the first and second sample (page 504, section under "Analysis of gene expression in lymphoid malignancies"); identifying a concordance set of expressed genes with the same direction of differential expression (i.e. identifying genes common to the first and second reference sets) (page 504 - page 505, section under "Gene expression patterns and

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tumor phenotype"). Furthermore, Alizadeh et al. recorded the subset of genes within a concordance set in a user-readable format (page 504, section under "Gene expression patterns and tumor phenotype" and Figure 2).

However, Alizadeh et al. do not teach determining a correlation coefficient that exceeds a predetermined value.

Regarding claim 1, Bertucci et al. teaches determining the correlation coefficient that exceed a predetermine value for correlating genes (page 2987, right column, 2<sup>nd</sup> full paragraph).

Regarding claims 2-6, Bertucci et al. teach determining a correlation coefficient (page 2987, right column, 2<sup>nd</sup> full paragraph); logarithmically transforming the differentials (page 2987, right column, 3<sup>rd</sup> full paragraph); wherein the correlation coefficient has an absolute value greater than 0.98 (page 2987, right column, 2<sup>nd</sup> full paragraph).

Regarding claims 8-11, Bertucci et al. teach wherein the gene expression data is cDNA or RNA quantification data (page 870); wherein the sample comprises of a cell line, which is a tumor cell line (page 869, left column, top).

Regarding claims 16-19, Bertucci et al. teach wherein the sample is from a patient, a healthy donor, is a tumor cell, or from the colon (paragraph bridging pages 869-867).

Regarding claim 20, Bertucci et al. teach where the phenotype is selected from lymph node status (page 2983, left column, bottom section).

Regarding claim 21, Bertucci et al. teach where a plurality of independent samples is used for each sample (paragraph bridging page 869-870); and where the differential is an average over the sample (page 870, Table II).

Regarding claim 22, Bertucci et al. teach determining a second correlation coefficient with a positive sign that establishes a positive correlation with a phenotype (page 2983, right column, first full paragraph).

Regarding claim 23, Bertucci et al. teach that ERBB2 had the highest correlation of the genes tested (page 2983, first full paragraph) and since its correlation was the highest its correlation was the most reliable indication of cancer (abstract; page 2985, left column, bottom paragraph – right column, top paragraph).

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the methods of Alizadeh et al. with Bertucci et al. to gain the advantage of determining the reproducibility of experiments. One of the challenges that face gene expression experiments is the precision of the equipment used in those experiments. Given the same experiment, the equipment may produce different results. Given the uncertainty of the equipment as well as the need to compare data from different sources, one of ordinary skill in the art would seek to verify the reproducibility of experiments to ensure that their interpretation of the data is correct. Bertucci et al. teaches a method of determining the accuracy of gene expression using a correlation coefficient (page 2987, right column, 2<sup>nd</sup> full paragraph). Thus, one of ordinary skill in the art would be motivated to combine the methods of Alizadeh et al. and Bertucci et al. to ensure that the gene expression data was accurate.

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Response to Arguments

6. Applicants have responded to this rejection by stating that Alizadeh et al. does not teach a second reference set. However, Alizadeh et al. teach measuring the gene expression between 96 normal and malignant samples (page 504, left column, bottom). The Examiner is interpreting each of these measurements as a separate reference set. Thus, Alizadeh et al. teach creating multiple reference sets. In addition, Alizadeh et al. teach that the samples are from different patients or different cell lines. Thus, Alizadeh et al. teach the samples are from a different source.

Applicants also state Bertucci et al.'s correlation coefficient is for a pair of genes and not two expression differentials. However a set of reference genes, as in the claims, may be broadly read include a single gene. Thus, the correlation coefficient of Bertucci et al. is within the scope of the claimed invention.

7. Claims 12 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Alizadeh et al. (Nature (2000) Volume 403, pages 503-511) in view of Bertucci et al. (Human Molecular Genetics (2000) Volume 9, Number 20, pages 2981-2991) further in view of Young et al. (US #2005/0255588 A1).

The instant claims are drawn to identifying a subset of genes using a correlation coefficient calculated from gene expression data and using samples comprising omnipotent or pluripotent cells.

Alizadeh et al. and Bertucci et al. are applied as above.

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However, neither Alizadeh et al. nor Bertucci et al. teach using pluripotent or omnipotent stem cells.

Young et al. teach creating samples of pluripotent or omnipotent stem cells (page 3, paragraph 0019-0020).

It would have been obvious to one of ordinary skill in the art at the time of the invention to use the cell lines described in Young et al. with the methods of Alizadeh et al. and Bertucci et al. The motivation to combine Alizadeh et al. with Bertucci et al. is provided above. It is recognized in the art the use of stem cells could potentially provide many new applications in science and medicine (Young et al., page 3, paragraph 0015-0016). However, it is unclear what genes are expressed to maintain a cell as a stem cell. Thus one of ordinary skill in the art seeking to understand the gene expression of stem cells would be motivated to determine what genes are differentially expressed that correspond to the stem cell phenotype. Alizadeh et al. provide a method of identifying the correct identification of the differences in gene expression between different cell lines (Alizadeh et al., page 504). Alizadeh et al.'s method could identify the differences in gene expression in a stem cell as compared to other cells. Thus one of ordinary skill in the art seeking to understand the gene expression of stem cells would be motivated to take the sample cell lines disclosed by Young et al. and use those samples in the method provided by Alizadeh et al.

#### Response to Arguments



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8. Applicants have responded to this rejection by relying on their arguments toward Alizadeh et al. and Bertucci et al. See above for the Examiner's response.

9. Claims 24-28 and 36-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Alizadeh et al. (Nature (2000) Volume 403, pages 503-511) in view of Bertucci et al. (Human Molecular Genetics (2000) Volume 9, Number 20, pages 2981-2991) in view of Horne et al. (US 6,974,667) in view of Dai et al. (US 7,171,311) in view of Ohara et al. (DNA Res. (1997) Volume 4, number 5, pages 345-349) in view of Bach (Nucleic Acids Research (1991) Volume 19, number 13, pages 3553-3559) in view of Volta et al. (Genomics (1999) Volume 55, number 1, pages 68-77) in view of Ohara et al. (DNA Res. (1998) Volume 5, number 3, pages 169-176) in view of Venter et al. (US 6,812,339), in view of Calabretta et al. (US 5,734,039), in view of Wohlgemuth et al. (US 6,905,827), in view of Cocks et al. (US 6,607,879).

Alizadeh et al. and Bertucci et al. are applied as above.

However, neither Barney et al. nor Blasband et al. teach using the genes listed in Table 69.

Horne et al. disclose the genes with the sequences of Seq ID 2240 (MGC5466), Seq ID 2249 (MGC5466), Seq ID 2254 (IER3) (see sequence search report).

Dai et al. disclose the genes with the sequences of Seq ID 2241 (Wnt5A), Seq ID 2245 (ITPR1), Seq ID 2250 (CHAF1A) (see sequence search report).

Ohara et al. (1997) discloses the gene AB007945 (i.e., KIAA0476, Seq ID 2243) (see NCBI printout).

Bach discloses the gene with the sequence of Seq ID 2247 (TCF2) (see sequence search report).

Volta et al. discloses the gene with the sequence of Seq ID 2252 (CDS2) (see sequence search report).

Ohara et al. (1998) discloses the gene of Seq ID 2256 (PPFIA3) (see ncbi search results).

Venter et al. discloses the gene of Seq ID 2258 (COPEB) (see sequence search report).

Calabretta et al. discloses the gene of Seq ID 2260 (FOS) (see sequence search report).

Wohlgemuth et al. discloses the gene of Seq ID 2262 (JUNB) (see sequence search report).

Cocks et al. discloses the gene of Seq ID 2264 (ZFP36) (see sequence search report).

It would have been obvious to one of ordinary skill in the art to combine the methods of Alizadeh et al. and Bertucci et al. with the probes for the genes of Horne et al. Dai et al., Ohara et al., Venter et al., Wohlgemuth et al. and Cocks et al. Each of the genes of Table 69 are known in the prior art as shown above. Given that Alizadeh et al. and Bertucci et al. both analyze gene expression levels on microarrays, one of ordinary skill in the art at the time of the invention could have substituted the genes used by Alizadeh et al. and Bertucci et al. with the genes of Table 69 for the predictable result of analyzing the gene expression levels of the genes of Table 69.

Response to Arguments

10. Applicants have responded to this rejection by relying on their arguments toward Alizadeh et al. and Bertucci et al. See above for the Examiner's response.

***Contact Information***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JERRY LIN whose telephone number is (571)272-2561. The examiner can normally be reached on 7:00-5:30pm, M-TH.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie A. Moran can be reached on (571) 272-0720. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jerry Lin/  
Examiner, Art Unit 1631  
1/20/09